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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,341	10/13/2000	Hisakazu Kurita	K0448/7003	5123

7590 10/20/2006

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,341	KURITA ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2006* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 13-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 13-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 08/01/2006.

Claims 1, 3-6 and 13-19 are pending and included in the prosecution.

The following new ground of rejection is necessitated by applicants' amendment:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3-6 and 13-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment made to claim 1 has introduced new matter that is not supported by the specification as originally filed and that is: "grinding a composition in the form of powder comprising an organic acid salt an a base drug salt to make a mean diameter of the organic acid salt 0.1-100 μm". Applicants are referring to example 11 on page 19 of the present specification for

support. Recourse to example 11, the example showed grinding powder ingredients only and not the composition as a whole. In addition, example 11 showed grinding in liquid paraffin only. Furthermore, example 11 that disclosed the grinding step shows only grinding of sodium acetate and fentanyl citrate, and disclosure of species in example 11 does not support the genus of claim 1 that recites any organic acid salt and any base drug salt. Examples 12 and 13 show that only sodium acetate was ground. Therefore, no support for the general concept of grinding composition comprising the organic salt and the salt of the basic drug as instantly claimed because the examples show that each drug is treated differently in term of grinding.

The following rejection was discussed in details in the previous office action and are maintained for reasons of record:

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 3-6, and 13-19 are rejected under 35 U.S.C. 102(a) as being anticipated by JP 10045570 ('570).

JP '570 discloses percutaneous adhesive preparation that has low skin irritation and excellent skin permeability (abstract). The preparation forms an adhesive layer comprising 0.05-20 wt.% of active agent and 0.01-15 wt.% of sodium acetate (abstract; claims 1, 2; page 2, paragraphs 0006, 0008). The adhesive layer is prepared by solvent method, or hot melt method followed by spreading and drying of the adhesive preparation on a base layer, i.e. backing (page 4, paragraphs 0014, 0015). The reference anticipates the claims because it discloses the same method of making the adhesive preparation using the same ingredients, resulting in a composition comprising the ion pairs of the drug with the organic acid salt in melted form or in ionically dissolved form in a solvent, with no powder or particle in the composition after either way of making. If the composition is produced by the dissolving method, the particles size is not important because the particle of any size will dissolve and form ion-pairs with the drug forming new complex particles. If the composition is produced by the hot-melting method, the particles size is not important because the particle of any size will melt and form ion-pairs with the drug forming new complex amorphous lump. Therefore, the reference anticipates the claims because the claims are directed to adhesive preparation comprising ion-pairs of basic drug with organic acid salt.

5. Claims 1, 3-6 and 13-19 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 08-157365 ('365).

JP '365 discloses a transdermal adhesive preparation having remarkable high skin permeation rate and remarkable reduced skin irritation and provides good medicine stability. The preparation forms an adhesive layer in a plaster comprising 0.1-10 wt.% base drug salt and 0.5-5 wt.% of sodium acetate (abstract; page 1 of the translation, claim 6; page 3, paragraph 009). The adhesive layer is prepared by solvent method, or hot melt method followed by spreading and drying of the adhesive preparation on a base layer, i.e. backing (page 4, paragraphs 0015, 0016). The reference anticipates the claims because it discloses the same method of making the adhesive preparation using the same ingredients, resulting in a composition comprising the ion pairs of the drug with the organic acid salt in melted form or in ionically dissolved form in a solvent, with no powder or particle in the composition after either way of making. If the composition is produced by the dissolving method, the particles size is not important because the particle of any size will dissolve and form ion-pairs with the drug forming new complex particles. If the composition is produced by the hot-melting method, the particles size is not important because the particle of any size will melt and form ion-pairs with the drug forming new complex amorphous lump. Therefore, the reference anticipates the claims because the claims are directed to adhesive preparation comprising ion-pairs of basic drug with organic acid salt.

6. Claims 1, 3-6, 13-19 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,866,157 ('157).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

US '157 discloses an adhesive composition for matrix patch formulation that improves the permeability of the drug and significantly reduces the skin irritation (col.2, lines 33-36). The adhesive composition forms a layer comprising from 0.1 to 20 % (w/w) of a basic drug and from 0.01 to 15 % (w/w) of organic acid or its salt such as sodium acetate (abstract; col.2, lines 40-60; col.3, lines 9-25, 55-58; examples). The adhesive layer is prepared by solvent method, or hot melt method followed by spreading and drying of the adhesive preparation on paper or backing (col.6, lines 3-16). The reference anticipates the claims because it discloses the same method of making the adhesive preparation using the same ingredients, resulting in a composition comprising the ion pairs of the drug with the organic acid salt in melted form or in ionically dissolved form in a solvent, with no powder or particle in the composition after either way of making. If the composition is produced by the dissolving method, the particles size is not important because the particle of any size will dissolve and form ion-pairs with the drug forming new complex particles. If the composition is produced by the hot-melting method, the particles size is not important because the particle of any size will melt and form ion-pairs with the drug forming new complex amorphous lump. Therefore, the reference

anticipates the claims because the claims are directed to adhesive preparation comprising ion-pairs of basic drug with organic acid salt.

Response to Arguments

7. Applicant's arguments filed 08/01/2006 have been fully considered but they are not persuasive. The main gist of applicants' argument against 102 rejections above is the cited references do not teach the step of grinding the powdered composition or the diameter of the particles.

In response to this argument, the examiner is pointing to paragraph 0022 of JP '570 where the reference disclosed that sodium acetate and fentanyl citrate are crushed. Regarding JP '365 and US '157, it is noticed that the claims are directed to a composition, and all the elements of the composition are disclosed by the references. The particle sizes is implied by the teachings of all the references as they disclose making a film having thickness of less than 100 μm and this implied the particle sizes of the ingredients should be less than 100 μm.

Regarding product by process claims, MPEP 2113 [R-1] states: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe,* 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (Claim was directed to a novolac color

developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product).

In the instant situation, the percutaneous preparation disclosed by any of the prior art is identical to the present percutaneous preparation. The cited prior art implied the particle sizes. The cited prior art provided improved percutaneous delivery of the drugs as desired by applicants. Hence, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3-6, and 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10045570 ('570).

JP '570 teaches percutaneous adhesive preparation that has low skin irritation and excellent skin permeability (abstract). The preparation forms an adhesive layer comprising 0.05-20 wt.% of active agent and 0.01-15 wt.% of sodium acetate (abstract; claims 1, 2; page 2, paragraphs 0006, 0008). The adhesive layer is prepared by solvent method, or hot melt method followed by spreading and drying of the adhesive preparation on a base layer, i.e. backing (page 4, paragraphs 0014, 0015). The reference discloses the same method of making the adhesive preparation using the same ingredients, resulting in a composition comprising the ion pairs of the drug with the organic acid salt in melted form or in ionically dissolved form in a solvent, with no powder or particle in the composition after either way of making. If the composition is produced by the dissolving method, the particles size is not important because the

particle of any size will dissolve and form ion-pairs with the drug forming new complex particles. If the composition is produced by the hot-melting method, the particles size is not important because the particle of any size will melt and form ion-pairs with the drug forming new complex amorphous lump.

The reference does not teach the mean diameter of the organic acid. The diameter of the organic acid does not impart patentability to the claims in absence of superior and unexpected results. The claims are directed to product by process, and the product is a drug forming ion-pairs with an organic acid salt. The process of production of the product included dissolving in a solvent method or heat melting method, and in either method the diameter of the particles of the organic acid salt is not important because the organic acid salt will either dissolve to form a solution or melt to form amorphous lump and then form the ion pair with the drug.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide an adhesive produced by dissolving in a solvent method or heat melting method of the drug and the salts of organic acid as disclosed by the reference, and select organic acid with small diameter motivated by the logic that smaller particles will dissolve or melt faster, with reasonable expectation of having an adhesive layer produced by dissolving or melting drug and salt of organic acid that less time consuming. In any event, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable / ranges involves only routine skill in the art. *In re Aller* 105 USPQ 233.

11. Claims 1, 3-6, and 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 08-157365 ('365).

JP '365 teaches a transdermal adhesive preparation having remarkable high skin permeation rate and remarkable reduced skin irritation and provides good medicine stability. The preparation forms an adhesive layer in a plaster comprising 0.1-10 wt.% base drug salt and 0.5-5 wt.% of sodium acetate (abstract; page 1 of the translation, claim 6; page 3, paragraph 009). The adhesive layer is prepared by solvent method, or hot melt method followed by spreading and drying of the adhesive preparation on a base layer, i.e. backing (page 4, paragraphs 0015, 0016). The reference discloses the same method of making the adhesive preparation using the same ingredients, resulting in a composition comprising the ion pairs of the drug with the organic acid salt in melted form or in ionically dissolved form in a solvent, with no powder or particle in the composition after either way of making. If the composition is produced by the dissolving method, the particles size is not important because the particle of any size will dissolve and form ion-pairs with the drug forming new complex particles. If the composition is produced by the hot-melting method, the particles size is not important because the particle of any size will melt and form ion-pairs with the drug forming new complex amorphous lump.

The reference does not teach the mean diameter of the organic acid. The diameter of the organic acid does not impart patentability to the claims in absence of superior and unexpected results. The claims are directed to product by process, and the product is a drug forming ion-pairs with an organic acid salt. The process of production

of the product included dissolving in a solvent method or heat melting method, and in either method the diameter of the particles of the organic acid salt is not important because the organic acid salt will either dissolve to form a solution or melt to form amorphous lump and then form the ion pair with the drug.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide an adhesive produced by dissolving in a solvent method or heat melting method of the drug and the salts of organic acid as disclosed by the reference, and select organic acid with small diameter motivated by the logic that smaller particles will dissolve or melt faster, with reasonable expectation of having an adhesive layer produced by dissolving or melting drug and salt of organic acid that less time consuming. In any event, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable / ranges involves only routine skill in the art. *In re Aller* 105 USPQ 233.

12. Claimss1, 3-6, and 13-19 are rejected under 35 U.S.C. 103(a) as being obvious over US 5,866,157 ('157).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject

matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

US '157 teaches an adhesive composition for matrix patch formulation that improves the permeability of the drug and significantly reduces the skin irritation (col.2, lines 33-36). The adhesive composition forms a layer comprising from 0.1 to 20 % (w/w) of a basic drug and from 0.01 to 15 % (w/w) of organic acid or its salt such as sodium acetate (abstract; col.2, lines 40-60; col.3, lines 9-25, 55-58; examples). The adhesive layer is prepared by solvent method, or hot melt method followed by spreading and drying of the adhesive preparation on paper or backing (col.6, lines 3-16). The reference discloses the same method of making the adhesive preparation using the same ingredients, resulting in a composition comprising the ion pairs of the drug with the organic acid salt in melted form or in ionically dissolved form in a solvent, with no powder or particle in the composition after either way of making. If the composition is produced by the dissolving method, the particles size is not important because the particle of any size will dissolve and form ion-pairs with the drug forming new complex particles. If the composition is produced by the hot-melting method, the particles size is

not important because the particle of any size will melt and form ion-pairs with the drug forming new complex amorphous lump.

The reference does not teach the mean diameter of the organic acid. The diameter of the organic acid does not impart patentability to the claims in absence of superior and unexpected results. The claims are directed to product by process, and the product is a drug forming ion-pairs with an organic acid salt. The process of production of the product included dissolving in a solvent method or heat melting method, and in either method the diameter of the particles of the organic acid salt is not important because the organic acid salt will either dissolve to form a solution or melt to form amorphous lump and then form the ion pair with the drug.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to provide an adhesive produced by dissolving in a solvent method or heat melting method of the drug and the salts of organic acid as disclosed by the reference, and select organic acid with small diameter motivated by the logic that smaller particles will dissolve or melt faster, with reasonable expectation of having an adhesive layer produced by dissolving or melting drug and salt of organic acid that less time consuming. In any event, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable / ranges involves only routine skill in the art. *In re Aller* 105 USPQ 233.

Applicants' arguments

13. Applicant's arguments filed 08/01/2006 have been fully considered but they are not persuasive. Applicants repeat the same argument regarding the grinding step to produce specific particle sizes. Applicants argue that they showed superior and unexpected results over the higher particle sizes.

In response to these arguments, applicants' attention is drawn to the scope of the claims that is directed to product by process, and the examiner is repeating the argument as in section 7 of this office action.

The claims are directed to composition and all the elements of the composition are disclosed by the cited references, basic drug and organic acid salt. The art recognized the suitability of the sodium acetate in increasing the dermal absorbability of active agents. The difference between the cited art and the present invention is the particle sizes that is implied by the teaching of all the references because JP 570 teaches crushing of sodium acetate and fentanyl citrate, and all the references teach making a film having thickness of less than 100 μm and this implied the particle sizes of the ingredients should be less than 100 μm. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have the claimed composition with a particle diameters of the organic acid salts ranging from 0.1 to 10 micrometers, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller* 105 USPQ 233. The cited references suggest the sodium acetate in the powder form as they all teach dissolving all the other components except for the sodium acetate that is dispersed in the mixture, JP '365 at page 7,

paragraph 0030; JP '570 at page 5, paragraphs 0020-0022; US '157 at co1.11, lines 61-64 and co1.12, lines 16-19. The cited references all teach the ion pair formation between the drug and the organic acid salts, JP '365 at page 3, paragraph 009; JP '570 at page 1, paragraph 0004; US '157 at co1.2, lines 10-11. Sodium acetate is a known as powder; see the "Condensed Medial Dictionary", page1007, 1008. It is known to one having ordinary skill in the art that the smaller the particle sizes the easier and more enhanced its transdermal absorption. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

With regard to the superior results provided by applicants' examples and comparative examples, and with careful review, the examiner has noticed that applicant did not show the effect of particle size at the upper and lower limits of the claimed range, i.e. particle diameter at 0.1 and at 10 100 μm. The examples use only specific

organic acid salt, i.e. sodium acetate, and it is not clear if other organic salts will have the same particle sizes and same effect on the percutaneous absorption of the drugs. The examples further contain other ingredients that significantly affect the percutaneous absorption of active agents, such as liquid paraffin, lauryl alcohol and propylene glycol. Therefore, no superior effect has been shown on the percutaneous absorption of base drug that ion paired with organic salt, without the influence of other ingredients.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. 5,629,019 disclosed that micronization of compounds accelerates their skin permeation.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

IG

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600